In re Application of: Joseph ITSKOVITZ-ELDOR et al
Serial No.: 10/536,734
Filed: May 27, 2005
Office Action Mailing Date: February 17, 2010

Examiner: Kim, Taeyoon
Group Art Unit: 1651
Attorney Docket: 29601
Confirmation No.: 3958

REMARKS

Reconsideration of the above-identified application in view of the amendments above and the remarks following is respectfully requested.

Claims 193, 194, 197, 199-201, 205 and 214-234 are in this Application. Claims 194, 201 and 216-234 have been withdrawn from consideration. Claims 193, 197, 199, 200, 205, 214 and 215 have been rejected.

35 U.S.C. § 103 Rejections

The Examiner has rejected claims 193, 197, 199, 200 and 205 under U.S.C. 103(a) as being unpatentable over Lumelsky et al. in view of Dang et al. in further view of Zhao et al. The Examiner has also rejected claims 193, 214 and 215 under U.S.C. 103(a) as being unpatentable over Lumelsky et al. in view of Dang et al. in further view of Zhao et al. and Thomson et al.

The Examiner's rejections are respectfully traversed.

The Examiner states that although Lumelsky et al. do not teach the cell selection step of the presently claimed invention (which leads to formation of surface bound clusters), Dang et al. teach cell dissociation for the purpose of performing flow cytometry and as such, it would have been obvious for a person of ordinary skill in the art at the time the invention was made to dissociate the EBs of Lumelsky et al. to obtain single cells and isolate cells having pancreatic progenitor phenotype at taught by Dang et al.

The Examiner further states that although Lumelsky et al. do not teach a step of dissociating surface bound clusters into single cells and forming suspension cultures to obtain suspended clusters of insulin secreting cells, Zhao et al. teach suspension cultures of islets and as such it would have been obvious to combine the method step of Zhao et al. in the method of Lumelsky et al. in view of Dang et al.

Examiner thus suggests that one of ordinary skill in the art would generate EBs according to the method of Lumelsky et al., isolate cells from the EBs according to the

method of Dang et al., take the cells of Dang et al. and apply the culturing conditions of Lumelsky et al. (though such conditions are not described in this context by Lumelsky et al.) to generate surface bound clusters (that are not described anywhere in the prior art) and finally apply Zhao et al. to isolate cells from the surface bound clusters and culture such cells to obtain suspended clusters and then isolate individual cells from the suspended clusters! Applicant contends that such a nexus does not exists in the prior art cited by the Examiner and would not be applied by an ordinary skilled artisan.

Previously presented claim 193 includes step (d) which teaches dissociation of the surface bound cell clusters of step (c) into single cells and culturing of the dissociated cells under non-adherent conditions to form suspended cell clusters (which are islet-like in appearance and include proliferating, non-apoptotic insulin-producing cells, see Figures 1g and 8a-d of the instant application). None of the prior art references cited by the Examiner suggest forming surface bound clusters from cells derived from EBs, followed by forming individual cells by dissociating such surface bound clusters followed by forming suspended clusters from individual cells derived from the surface bound clusters.

As was argued in the previous response, the present inventors unexpectedly discovered (see section [0322] of the published application) that the addition of step (d) lead to an unexpected formation of the suspended cell clusters and an unexpected increase in the proportion of insulin secreting cells relative to the clusters formed in step (c).

It will be appreciated that even if one of ordinary skill in the art combined Lumelsky et al. with Dang et al. to dissociate EBs into individual cells and culture such EB-derived cells to form the surface bound clusters of step (c) nothing in the teachings of Lumelsky et al., Dang et al. or Zhao et al. suggest that dissociation of the surface bound clusters of step (c) into individual cells and culturing such cells would lead to formation of insulin-producing suspended clusters.

Zhao et al. state that "The objective of this study was to examine an in vitro method for preserving the capacity of adult human beta cells to express insulin" (abstract). This study of Zhao et al. utilized cultured islets isolated from cadavers and not stem cells or islet progenitor cells. Zhao et al. do not teach generation of islets from stem cells but rather approaches for "long-term maintenance of the phenotype of beta cells in vitro". Applicant fails to see what in the teachings of Zhao et al. would motivate the ordinary skilled artisan to dissociate surface bound clusters (which are not taught by Zhao et al. or in Lumelsky et al. and Dang et al.) into individual cells and then culture such individual cells to obtain insulin-producing suspended clusters.

It will be appreciated that the present invention is not merely defined by the claimed method steps but also in the sequence of steps leading to the formation of the suspended clusters. Clearly there is no suggestion in the prior art of the combination and sequence of steps of claim 193.

The Examiner suggests that such a sequence of steps would be obvious to the ordinary skilled artisan since Lumelsky et al. teach EBs, Dang et al. teach isolation of cells from EBs and Zhao et al. teach suspended islet-like clusters. However, it appears that the Examiner disregarded the how and why of such a combination since the prior art does not provide the technical or motivational support necessary to make the present invention. Combining these references without such support clearly constitutes impermissible hindsight.

As such, Applicant strongly believes that the prior art of record does not render obvious the present invention as claimed.

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In view of the above amendments and remarks it is respectfully submitted that claims 193, 197, 199, 200, 205, 214 and 215 are now in condition for allowance. A prompt notice of allowance is respectfully and earnestly solicited.

Respectfully submitted,

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